in liposomes containing lipid A have been shown to induce humoral effectors (i.e., antigen-specific antibodies), and some have been shown to induce cell-mediated responses as well. Generation of an immune response and immunoprotection in an animal vaccinated with a malaria antigen may be assayed by immunofluorescence to whole, fixed malaria sporozoites or CTLs killing of target cells transfected with CSP.

IN THE CLAIMS

Kindly enter the following amended claims.

1. (Amended Twice) A method of inducing an immune response comprising:

(a) applying a formulation to intact skin of an organism, wherein the formulation comprises (i) at least one antigen which is derived from a pathogen and (ii) at least one adjuvant comprising an ADP-ribosylating exotoxin or derivative thereof having adjuvant activity, and an effective amount of the antigen which is not encapsulated induces the immune response;

(b) activating a Langerhans cell with the at least one adjuvant; and

(c) presenting the at least one antigen or epitope thereof on a cell surface of the Langerhans cell to a lymphocyte, thereby inducing the immune response in the organism.

2. (Amended Twice) The method of claim 1, wherein the formulation consists essentially of antigen and adjuvant.

4. (Amended Twice) The method of claim 1, wherein a physical, chemical, electrical, or sonic penetration enhancer is not used.

11. (Amended) The method of claim 1, wherein the antigen is derived from a bacterium.

12. (Amended) The method of claim 1, wherein the antigen is derived from a virus.

B4

13. (Amended) The method of claim 1, wherein the antigen is derived from a fungus or parasite.

B5

15. (Amended) The method of claim 1, wherein the formulation comprises a live or an attenuated live virus or virosome; and the antigen is expressed by the live or attenuated live virus or virosome, which is not encapsulated.

Ins C2

B6

22. (Amended Twice) The method of claim 1, wherein the ADP-ribosylating exotoxin is pertussis toxin or a derivative thereof having adjuvant activity.

23. (Amended Twice) The method of claim 1, wherein the ADP-ribosylating exotoxin is cholera toxin (CT) or a derivative thereof having adjuvant activity.

24. (Amended Twice) The method of claim 1, wherein the ADP-ribosylating exotoxin is *E. coli* heat-labile enterotoxin (LT) or a derivative thereof having adjuvant activity.

25. (Amended Twice) The method of claim 1, wherein the ADP-ribosylating exotoxin is diphtheria toxin (DT) or a derivative thereof having adjuvant activity.

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26. (Amended) The method of claim 1, wherein the ADP-ribosylating exotoxin is *Pseudomonas* exotoxin A or a derivative thereof having adjuvant activity.

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27. (Amended) The method of claim 1, wherein the formulation is a cream or gel or emulsion or ointment.

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B8

30. (Amended Twice) A method of immunization comprising applying a formulation to intact skin of an organism, wherein the formulation consists essentially of one or more ADP-ribosylating exotoxins or derivatives thereof having adjuvant activity,

and an effective amount of said one or more ADP-ribosylating exotoxins or derivatives thereof is not encapsulated.

31. (Amended) A method of inducing an immune response comprising:

(a) applying a formulation to intact skin of an organism, wherein the formulation comprises (i) at least one antigen which is derived from a pathogen and (ii) at least one ADP-ribosylating exotoxin or derivative thereof having adjuvant activity, and at least some antigen which is not encapsulated induces the immune response; and

(b) inducing the immune response in the organism without perforating the skin, wherein the immune response is specific for the antigen.

32. (Amended Twice) A method of inducing an immune response comprising:

(a) applying a formulation to intact skin of an organism, wherein the formulation comprises (i) at least one antigen which is derived from a pathogen and (ii) at least one ADP-ribosylating exotoxin or derivative thereof having adjuvant activity, and at least some antigen which is not encapsulated induces the immune response;

(b) activating an antigen presenting cell with the at least one ADP-ribosylating exotoxin or derivative therof; and

(c) presenting the at least one antigen or epitope thereof on a cell surface of the antigen presenting cell to a lymphocyte, thereby inducing the immune response in the organism.

33. (Amended) A method of inducing an immune response comprising:

(a) applying epicutaneously on an organism an effective amount of at least one antigen derived from a pathogen and which is not encapsulated,

(b) activating a Langerhans cell underlying the organism's skin with at least one ADP-ribosylating exotoxin or derivative thereof having adjuvant activity,

(c) signaling the Langerhans cell to migrate to a lymph node of the organism and mature into a dendritic cell, and

(d) presenting the at least one antigen or epitope thereof on a cell surface of the dendritic cell to a lymphocyte; thereby inducing the immune response in the organism, wherein the immune response is specific for the at least one antigen.

Kindly delete claims 36-40 without prejudice or disclaimer.

Kindly enter the following new claims.

50 ~~41~~. (New) The method of claim 1, wherein the formulation comprises an ADP-ribosylating exotoxin derivative which is less toxic but remains immunogenic.

51 ~~42~~. (New) The method of claim 1, wherein the formulation comprises a genetically produced derivative of ADP-ribosylating exotoxin in which ADP-ribosyl transferase activity is inactivated.

52 ~~43~~. (New) The method of claim 1, wherein the formulation comprises a chemically produced derivative of ADP-ribosylating exotoxin in which ADP-ribosyl transferase activity is inactivated.

53 ~~44~~. (New) The method of claim 1, wherein the formulation comprises an ADP-ribosylating exotoxin B subunit.

54 ~~45~~. (New) The method of claim 1, wherein the formulation is comprised of antigen molecules as chemical or recombinant conjugates.

55 ~~46~~. (New) The method of claim 1, wherein the formulation is comprised of a single molecule containing both antigen and adjuvant properties.

56 ~~47~~. (New) The method of claim 1, wherein the formulation is comprised of at least some antigen molecules which lack adjuvant properties.

57 ~~48~~. (New) The method of claim 1, wherein the antigen has a molecular weight greater than 800 daltons.

58 ~~49~~. (New) The method of claim 1, wherein the antigen has a molecular weight greater than 1000 daltons.

Ins C4

59 ~~50~~. (New) The method of claim 1, wherein the antigen is a polypeptide of greater than 800 daltons molecular weight.

60 ~~51~~. (New) The method of claim 1, wherein the antigen is a polypeptide of greater than 1000 daltons molecular weight.

B12 and D7

61 ~~52~~. (New) The method of claim 1, wherein the formulation comprises a whole organism, and the antigen is expressed by the whole organism which is not encapsulated.

Ins C5

62 ~~53~~. (New) A method of immunization comprising applying a formulation without lipid vesicles to intact skin of an organism, wherein the formulation is comprised of an effective amount of one or more ADP-ribosylating exotoxins or derivatives thereof having adjuvant activity.

63 ~~54~~. (New) The method of claim 53, wherein an allergic reaction is not induced by the immunization method.

64 ~~55~~. (New) The method of claim 53 further comprising applying alcohol to the intact skin prior to application of the formulation.

65 ~~56~~. (New) The method of claim 53 further comprising hydrating the intact skin prior to application of the one or more ADP-ribosylating exotoxins or derivatives thereof.

66 ~~57~~. (New) The method of claim 53, wherein the formulation is a solution or suspension.

67 ~~58~~. (New) The method of claim 53, wherein the formulation is a cream or gel or emulsion or ointment.

68 ~~59~~. (New) The method of claim 53, wherein the formulation is applied with a patch.

69 ~~60~~. (New) The method of claim 53, wherein at least one of the ADP-ribosylating exotoxins is pertussis toxin.

B12

70 ~~61~~. (New) The method of claim 53, wherein at least one of the ADP-ribosylating exotoxins is cholera toxin.

71 ~~62~~. (New) The method of claim 53, wherein at least one of the ADP-ribosylating exotoxins is *E. coli* heat-labile enterotoxin.

72 ~~63~~. (New) The method of claim 53, wherein at least one of the ADP-ribosylating exotoxins is diphtheria toxin.

73 ~~64~~. (New) The method of claim 53, wherein at least one of the ADP-ribosylating exotoxins is *Pseudomonas* exotoxin A.

74 ~~65~~. (New) The method of claim 53, wherein the formulation comprises an ADP-ribosylating exotoxin derivative which is less toxic but remains immunogenic.

75 ~~66~~. (New) The method of claim 53, wherein the formulation comprises a genetically produced derivative of ADP-ribosylating exotoxin in which ADP-ribosyl transferase activity is inactivated.

76 ~~67~~. (New) The method of claim 53, wherein the formulation comprises a chemically produced derivative of ADP-ribosylating exotoxin in which ADP-ribosyl transferase activity is inactivated.

B12

77 ~~68~~. (New) The method of claim 53, wherein the formulation comprises an ADP-ribosylating exotoxin B subunit.

Ins C6

78 ~~69~~. (New) A method of immunization comprising hydrating intact skin of an organism; applying an effective amount of one or more ADP-ribosylating exotoxins or derivatives thereof having adjuvant activity to the hydrated, intact skin in the absence of lipid vesicles; and separately administering one or more antigens which are derived from one or more pathogens such that the organism is effectively immunized.

ADD C7

IN THE SEQUENCE LISTING

Kindly enter the attached paper and computer readable forms of the Sequence Listing.